27. An isolated nucleic acid molecule comprising a nucleotide sequence of the formula: R^1-R^2-R^3-R^4, wherein

R^1 is ATG, or the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), or is absent;

R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7) or is absent;

R^3 is the nucleotide sequence of SEQ ID NO: 3; and

R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9) or is absent.

28. The isolated nucleic acid molecule of Claim 27, wherein R^1 is ATG, R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

29. The isolated nucleic acid molecule of Claim 27, wherein R^1 is ATG, R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R^4 is absent.

30. The isolated nucleic acid molecule of Claim 27, wherein R^1 is ATG, R^2 is absent, and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

31. The isolated nucleic acid molecule of Claim 27, wherein R^1 is ATG, R^2 is absent, and R^4 is absent.

32. The isolated nucleic acid molecule of Claim 27, wherein R^1 is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG

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GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

33. The isolated nucleic acid molecule of Claim 27, wherein R^1 is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R^4 is absent.

34. The isolated nucleic acid molecule of Claim 27, wherein R^1 is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R^2 is absent, and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

35. The isolated nucleic acid molecule of Claim 27, wherein R^1 is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R^2 is absent, and R^4 is absent.

36. The isolated nucleic acid molecule of Claim 27, wherein R^1 is absent, R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

37. The isolated nucleic acid molecule of Claim 27, wherein R^1 is absent, R^2 is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO:

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7), and R^4 is absent.

38. The isolated nucleic acid molecule of Claim 27, wherein R^1 is absent, R^2 is absent, and R^4 is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

39. The isolated nucleic acid molecule of Claim 27, wherein R^1 is absent, R^2 is absent, and R^4 is absent.

40. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

41. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4, wherein

R^1 is methionine, or the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), or is absent;

R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8) or is absent;

R^3 is the amino acid sequence of SEQ ID NO: 4; and

R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10) or is absent; and

wherein said polypeptide has:

a) at least one conservative amino acid substitution;

b) at least one amino acid substitution at a glycosylation site;

c) at least one amino acid substitution at a proteolytic cleavage site;

d) at least one amino acid substitution at a cysteine residue;

e) at least one amino acid deletion;

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f) at least one amino acid insertion;

g) a C- and/or N-terminal truncation; or

h) a combination of modifications selected from the group consisting of conservative amino acid substitutions, amino acid substitutions at a glycosylation site, amino acid substitutions at a proteolytic cleavage site, amino acid substitutions at a cysteine residue, amino acid deletions, amino acid insertions, C-terminal truncation, and N-terminal truncation.

42. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one conservative amino acid substitution.

43. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one amino acid substitution at a glycosylation site.

44. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one amino acid substitution at a proteolytic cleavage site.

45. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one amino acid substitution at a cysteine residue.

46. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one amino acid deletion.

47. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1–R^2–R^3–R^4 and has at least one amino acid insertion.

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48. The isolated nucleic acid molecule of Claim 41, wherein said polypeptide comprises an amino acid sequence of the formula: R^1-R^2-R^3-R^4 and has a C- and/or N-terminal truncation.

49. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide comprises an amino acid sequence of the formula: R^1-R^2-R^3-R^4, wherein

R^1 is methionine, or the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), or is absent;

R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8) or is absent;

R^3 is the amino acid sequence of SEQ ID NO: 4; and

R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10) or is absent.

50. The isolated nucleic acid molecule of Claim 49, wherein R^1 is methionine, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

51. The isolated nucleic acid molecule of Claim 49, wherein R^1 is methionine, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is absent.

52. The isolated nucleic acid molecule of Claim 49, wherein R^1 is methionine, R^2 is absent, and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

53. The isolated nucleic acid molecule of Claim 49, wherein R^1 is methionine, R^2 is absent, and R^4 is absent.

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54. The isolated nucleic acid molecule of Claim 49, wherein R^1 is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

55. The isolated nucleic acid molecule of Claim 49, wherein R^1 is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is absent.

56. The isolated nucleic acid molecule of Claim 49, wherein R^1 is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R^2 is absent, and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

57. The isolated nucleic acid molecule of Claim 49, wherein R^1 is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R^2 is absent, and R^4 is absent.

58. The isolated nucleic acid molecule of Claim 49, wherein R^1 is absent, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

59. The isolated nucleic acid molecule of Claim 49, wherein R^1 is absent, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is absent.

60. The isolated nucleic acid molecule of Claim 49, wherein R^1 is absent, R^2 is absent,

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and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

61. The isolated nucleic acid molecule of Claim 49, wherein R^1 is absent, R^2 is absent, and R^4 is absent.

62. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

63. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or a C- and/or N-terminally shortened sequence thereof.

64. The isolated nucleic acid molecule of Claim 63, wherein said polypeptide further comprises an amino-terminal methionine.

65. The isolated nucleic acid molecule of Claim 63, wherein said polypeptide comprises a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

66. The isolated nucleic acid molecule of Claim 65, wherein said polypeptide further comprises an amino-terminal methionine.

67. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO: 4.

68. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

69. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind

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TNF, wherein said polypeptide consists of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

70. An isolated nucleic acid molecule encoding a polypeptide having the ability to bind TNF, wherein said polypeptide consists of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

71. The nucleic acid molecule of either Claim 41 or 49, wherein said nucleic acid molecule encodes a polypeptide having at least one additional amino acid at the amino-terminus, at the carboxyl-terminus, or at both the amino-terminus and the carboxyl-terminus.

72. The nucleic acid of Claim 71, wherein said nucleic acid molecule encodes a polypeptide having at least one additional amino acid at the amino-terminus.

73. The nucleic acid of Claim 72, wherein said nucleic acid molecule encodes a polypeptide having a methionine at the amino-terminus.

74. The nucleic acid of Claim 71, wherein said nucleic acid molecule encodes a polypeptide having at least one additional amino acid at the carboxyl-terminus.

75. A nucleic acid that hybridizes under moderately or highly stringent conditions to the complement of the nucleic acid molecule of Claim 40.

76. A vector comprising the nucleic acid molecule of any of Claims 27, 41, 49, 63, 64, or 68.

77. A vector comprising the nucleic acid molecule of Claim 27.

78. A vector comprising the nucleic acid molecule of Claim 41.

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79. A vector comprising the nucleic acid molecule of Claim 49.

80. A vector comprising the nucleic acid molecule of Claim 63.

81. A vector comprising the nucleic acid molecule of Claim 64.

82. A vector comprising the nucleic acid molecule of Claim 68.

83. The vector of Claim 76, wherein said vector is an expression vector.

84. The vector of Claim 83, wherein said nucleic acid molecule comprises promoter DNA.

85. The vector of Claim 76, wherein said vector is replicable in a prokaryotic cell.

86. The vector of Claim 85, wherein the prokaryotic cell is *Escherichia coli*.

87. A vector comprising the nucleic acid molecule of Claim 66.

88. A vector comprising the nucleic acid molecule of Claim 70.

89. The vector of Claim 76, wherein said vector is replicable in a eukaryotic cell.

90. The vector of Claim 89, wherein the eukaryotic cell is a mammalian cell.

91. The vector of Claim 90, wherein the mammalian cell is a Chinese Hamster Ovary cell or a COS cell.

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92. A vector that is replicable in a Chinese Hamster Ovary cell, and wherein said vector comprises the nucleic acid molecule of Claim 62.

93. A vector that is replicable in a Chinese Hamster Ovary cell, and wherein said vector comprises the nucleic acid molecule of Claim 65.

94. A vector that is replicable in a Chinese Hamster Ovary cell, and wherein said vector comprises the nucleic acid molecule of Claim 67.

95. A vector that is replicable in a Chinese Hamster Ovary cell, and wherein said vector comprises the nucleic acid molecule of Claim 69.

96. The vector of Claim 89, wherein the eukaryotic cell is a yeast cell.

97. A recombinant host cell comprising the vector of Claim 76.

98. A recombinant host cell comprising the vector of Claim 87.

99. A recombinant host cell comprising the vector of Claim 88.

100. A recombinant host cell comprising the vector of Claim 92.

101. A recombinant host cell comprising the vector of Claim 93.

102. A recombinant host cell comprising the vector of Claim 94.

103. A recombinant host cell comprising the vector of Claim 95.

104. A recombinant host cell comprising the recombinant nucleic acid molecule of any of

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Claims 27, 41, 49, 63, 64, or 68.

105. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide further comprising an amino-terminal methionine.

106. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 4.

107. The recombinant host cell of Claim 106, wherein said recombinant nucleic acid molecule encodes a polypeptide further comprising an amino-terminal methionine.

108. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide comprising a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

109. The recombinant host cell of Claim 108, wherein said recombinant nucleic acid molecule encodes a polypeptide further comprising an amino-terminal methionine.

110. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 4.

111. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

112. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide consisting of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

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113. The recombinant host cell of Claim 104, wherein said recombinant nucleic acid molecule encodes a polypeptide consisting of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

114. The recombinant host cell of either Claims 97 or 104, wherein the recombinant host cell is a prokaryotic cell.

115. The recombinant host cell of Claim 114, wherein the prokaryotic cell is *Escherichia coli*.

116. The recombinant host cell of Claim 105, wherein the prokaryotic cell is *Escherichia coli*.

117. The recombinant host cell of Claim 107, wherein the prokaryotic cell is *Escherichia coli*.

118. The recombinant host cell of Claim 109, wherein the prokaryotic cell is *Escherichia coli*.

119. The recombinant host cell of Claim 111, wherein the prokaryotic cell is *Escherichia coli*.

120. The recombinant host cell of Claim 113, wherein the prokaryotic cell is *Escherichia coli*.

121. The recombinant host cell of either Claims 97 or 104, wherein the recombinant host cell is a eukaryotic cell.

122. The recombinant host cell of Claim 104, wherein the eukaryotic cell is a mammalian

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cell.

123. The recombinant host cell of Claim 122 wherein the mammalian cell is a Chinese Hamster Ovary cell or a COS cell.

124. The recombinant host cell of Claim 106, wherein the eukaryotic cell is a Chinese Hamster Ovary cell.

125. The recombinant host cell of Claim 108, wherein the eukaryotic cell is a Chinese Hamster Ovary cell.

126. The recombinant host cell of Claim 110, wherein the eukaryotic cell is a Chinese Hamster Ovary cell.

127. The recombinant host cell of Claim 112, wherein the eukaryotic cell is a Chinese Hamster Ovary cell.

128. The recombinant host cell of Claim 104, wherein the eukaryotic cell is a yeast cell.

129. The recombinant host cell of Claim 104, wherein the recombinant nucleic acid comprises promoter DNA other than the promoter DNA for SEQ ID NO: 1.

130. The recombinant host cell of Claim 104, wherein the recombinant host cell contains a heterologous promoter operationally linked to a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 2, and wherein a translation termination codon is positioned immediately after the asparagine at position 201.

131. A process of producing a recombinant polypeptide having the ability to bind TNF comprising culturing the recombinant host cell of either Claims 97 or 104 under suitable conditions

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to express the polypeptide.

132. A process comprising culturing the recombinant host cell of either Claims 97 or 104 under suitable conditions to amplify the nucleic acid molecule.

133. The process of Claim 131, wherein the recombinant host cell is a prokaryotic cell.

134. The process of Claim 133, wherein the prokaryotic cell is *Escherichia coli*.

135. The process of Claim 131, wherein the recombinant host cell is a eukaryotic cell.

136. The process according to Claim 135, wherein the host cell is the host cell of Claim 119.

137. The process according to Claim 135, wherein the host cell is the host cell of Claim 120.

138. The process of Claim 135, wherein the eukaryotic cell is a mammalian cell.

139. The process of Claim 138, wherein the mammalian cell is a Chinese Hamster Ovary cell or a COS cell.

140. The process according to Claim 135, wherein the host cell is the host cell of Claim 124.

141. The process according to Claim 135, wherein the host cell is the host cell of Claim 125.

142. The process according to Claim 135, wherein the host cell is the host cell of Claim

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126.

143. The process according to Claim 135, wherein the host cell is the host cell of Claim 127.

144. The process of Claim 135, wherein the eukaryotic cell is a yeast cell.

145. The process of Claim 131, wherein said polypeptide is expressed as a multimer.

146. The process of Claim 131, further comprising recovering the polypeptide from the culture.

147. The process of Claim 146, further comprising chemically derivatizing the recovered polypeptide.

148. The process of either Claim 146 or 147, wherein said recovered polypeptide is formulated to comprise said polypeptide and a pharmaceutically acceptable carrier.

REMARKS

Applicants contend that no new matter has been added as a result of the above-described amendments. Applicants respectfully request that the Examiner direct any inquiries regarding this communication to the undersigned representative at (312) 913-0001.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

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